CHIRAL RHENIUM AND RHODIUM COMPLEXES OF ANTICANCER AND ANTIBACTERIAL ACTIVITY: SYNTHESIS, ACTIVITY, AND PHYSICOCHEMICAL PROPERTIES

This project addresses two challenges of modern medicinal chemistry: the preselection of new agents for fighting (1) cancer and (2) microbial infections. Oncological research struggles with the acute side effects of conventional treatments such as Pt-based drugs. The 21st century enters into a "post-antibiotic era" when even mild infections can cause death after exposure to bacteria resistant to all available drugs (AMR). Our preliminary studies recognized a group of Rhenium and Rhodium complexes with promising anticancer activity against selected cancer cell lines and antibacterial activity against reference and clinical strains. These facts motivated us to study the new Re/Rh complexes in three cooperating institutions National Medicines Institute (NMI), Siedlce University of Natural Sciences and Humanities (UPH), and the Institute of Nuclear Chemistry and Technology (INCT).

MOTIVATION FOR THE PROJECT

(1) There is a need to systematically check potential anticancer (chiral) non-Pt metal complexes towards the cancer cell lines and harmful bacteria.
(2) Anticancer activity of some Re/Rh complexes is documented. Re is a ^{99m}Tc surrogate, and anticancer activity is transferable between Re and Tc complexes which can be used as radiotheranostics. The square-planar Rh complexes could act analogously to cisplatin but can exhibit lower toxicity.
(3) Antimicrobial activity of the new (chiral) Re/Rh complexes can be “highly significant” and thus contribute to finding a chemotherapeutic(s) against AMR bacteria.
(4) Comprehensive collection of structural and spectroscopic data gathered in the project can be used to predict desired properties in the design of new biologically active compounds.

THE MAIN AIMS OF THE PROJECT is to select candidates for non-Pt anticancer and/or AMR fighting agents. To this aim, we will: (1) Synthesize new chiral Re/Rh complexes and collect their structural and spectroscopic profiles; (2) Evaluate their anticancer activity using selected cancer/normal cell lines; (3) Determine antibacterial activity on reference/clinical strains; (4) Determine cellular pharmacokinetics and target sites in cells/bacteria.

THE PROBLEM TO BE SOLVED is the optimization of the Re/Rh complexes to maximize activity towards:
(1) selected cancer cell lines while minimizing against normal ones,
(2) reference and selected clinical bacterial strains,
Optimal interaction with cells/bacteria.
PROJECT'S RESEARCH WORKING HYPOTHESES are that the new chiral Re/Rh complexes will exhibit:
H 1. activity and selectivity against certain cancer cell lines,
H 2. activity and selectivity against specific reference and clinical bacterial strains,
H 3. cellular uptake sufficient for achieving effective pharmacological effect in cancer cells and/or bacteria ,
H 4. eminent properties for potential medical and non-medical applications.

THE EXPECTED EFFECT OF THE PROJECT

We will develop new chiral Re/Rh complexes:
(1) of significant anticancer but weak normal cell toxicity,
(2) of meaningful antibacterial activity,
(3) with precisely determined intracellular target sites and molecular action mechanisms,
(4) adequate for radiopharmacy/radiotheranostic,
(5) which will enrich our knowledge of the physicochemistry of chiral inorganics,
(6) PhDs devoted to anticancer activity and optical bioimaging (NMI), as well as physicochemical profile (INCT) will be completed, and vital material for Dr. Łyczko D.Sc. thesis (INCT) will be collected,
(7) patent applications for active compounds and articles will be published.